

Therapeutic Eradication of Cancer Stem Cells with UC-g61 (Cirmtuzumab)

Grant Award Details

Therapeutic Eradication of Cancer Stem Cells with UC-g61 (Cirmtuzumab)

Grant Type: Disease Team Therapy Development III

Grant Number: DR3-06924

Project Objective: Carry out and complete Phase 1/2 clinical trial in CLL patients with a ROR1 monoclonal antibody.

Investigator:

Name: Thomas Kipps
Institution: University of California, San Diego
Type: PI

Name: Catriona Jamieson
Institution: University of California, San Diego
Type: Co-PI

Disease Focus: Blood Cancer, Cancer

Human Stem Cell Use: Cancer Stem Cell

Award Value: \$4,179,598

Status: Active

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: Therapeutic Eradication of Cancer Stem Cells

Public Abstract: Cancer is a leading cause of death in California. Research has found that many cancers can spread throughout the body and resist current anti-cancer therapies because of cancer stem cells, or CSC. CSC can be considered the seeds of cancer; they can resist being killed by anti-cancer drugs and can lay dormant, sometimes for long periods, before growing into active cancers at the original tumor site, or at distant sites throughout the body. Required are therapies that can kill CSC while not harming normal stem cells, which are needed for making blood and other cells that must be replenished. We have discovered a protein on the surface of CSC that is not present on normal cells of healthy adults. This protein, called ROR1, ordinarily is found only on cells during early development in the embryo. CSC have co-opted the use of ROR1 to promote their survival, proliferation, and spread throughout the body. We have developed a monoclonal antibody that is specific for ROR1 and that can inhibit these functions, which are vital for CSC. Because this antibody does not bind to normal cells, it can serve as the "magic bullet" to deliver a specific hit to CSC. We will conduct clinical trials with the antibody, first in patients with chronic lymphocytic leukemia to define the safety and best dose to use. Then we plan to conduct clinical trials involving patients with other types of cancer. To prepare for such clinical trials, we will use our state-of-the-art model systems to investigate the best way to eradicate CSC of other intractable leukemias and solid tumors. Finally, we will investigate the potential for using this antibody to deliver toxins selectively to CSC. This selective delivery could be very active in killing CSC without harming normal cells in the body because they lack expression of ROR1. With this antibody we can develop curative stem-cell-directed therapy for patients with any one of many different types of currently intractable cancers.

Statement of Benefit to California:

The proposal aims to develop a novel anti-cancer-stem-cell (CSC) targeted therapy for patients with intractable malignancies. This therapy involves use of a fully humanized monoclonal antibody specific for a newly identified, CSC antigen called ROR1. This antibody was developed under the auspices of a CIRM disease team I award and is being readied for phase I clinical testing involving patients with chronic lymphocytic leukemia (CLL). Our research has revealed that the antibody specifically reacts with CSC of other leukemias and many solid-tumor cancers, but does not bind to normal adult tissues. Moreover, it has functional activity in blocking the growth and survival of CSC, making it ideal for directing therapy intended to eradicate CSC of many different cancer types, without affecting normal adult stem cells or other normal tissues. As such, treatment could avoid the devastating physical and financial adverse effects associated with many standard anti-cancer therapies. Also, because this therapy attacks the CSC, it might prove to be a curative treatment for California patients with any one of a variety different types of currently intractable cancers.

Beyond the significant benefit to the patients and families that are dealing with cancer, this project will also strengthen the position of the California Institute of Regenerative Medicine as a leader in cancer stem cell biology, and will deliver intellectual property to the state of California that may then be licensed to pharmaceutical companies.

In summary, the benefits to the citizens of California from the CIRM disease team 3 grant are:

- (1) Direct benefit to the thousands of patients with cancer
- (2) Financial savings through definitive treatment that obviates costly maintenance or salvage therapies for patients with intractable cancers
- (3) Potential for an anti-cancer therapy with a high therapeutic index
- (4) Intellectual property of a broadly active uniquely targeted anti-CSC therapeutic agent.

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